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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,921	09/22/2003	Dusan Miljkovic	100700.0011US2	3331

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EXAMINER	
BADR, HAMID R	

ART UNIT	PAPER NUMBER
1794	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,921	MILJKOVIC ET AL.	
	Examiner	Art Unit	
	HAMID R. BADR	1794	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant Amendments filed on 9/22/2008 is acknowledged.

Claims 1-20 are being considered on the merits.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 1 and 14 are indefinite for the phrase " conversion of one or more products in the fermentation medium to a desired product by the microorganism". While the conversion of a substrate to a product in a fermentation process is the logical pathway, the conversion of one or more "products" in the fermentation medium to a desired "product" is ambiguous and indefinite. It is unclear what is meant by the conversion of one product to another product. It is unclear what the applicants regard as the invention.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-5, 8-9, and 14-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Romanow et al. (1969, Effect of synthetic cytokinins on growth and pigment formation by *Rhodospirllum rubrum*; hereinafter R1, Examiner's Translation)

6. R1 discloses the effect of synthetic cytokinins, kinetin and 6-benzyladenine on growth of *R. rubrum*. Both of cytokinins accelerated growth for at least 4 days with 6-benzyladenine having the greater effect (Abstract).

7. R1 discloses that a strain of Rhodospirillum rubrum develops very well without yeast extract in the presence of kinetine and 6-benzyladenine at 10^{-5} to 10^{-14} g/ml (page 243, Materials and Methods).

8. R1 teaches that the aerobic culture, in solid or liquid media, is incubated at 28C. The anaerobic culture is done in liquid medium in tubes at 25-30C under light of 2000 lux intensity. To compare the growth of cultures due to the action of different quantities of cytokinin, R1 measures the absorption at 650 nm using a spectrophotometer. Spectral analysis of pigments of Rhodospirillum is performed by measuring absorption at 350-1000 nm by a live cell suspension. (page 244 paragraphs 1, 2, and 3).

9. R1 observes the aerobic culture during 3 days for those samples with or without yeast extract and with kinetine or 6-benzyladenine at different concentrations. (page 244, Results, first paragraph). The culture on solid culture neither grew well nor produced pigments. The liquid cultures were studied after 4 and 7 days by measuring absorbance at 650 nm. After 4 days R1 observes a stimulation of growth of the microorganism by both kinetine and by 6-benzyl adenine (page 244 last paragraph to

page 245 line 1). Photosynthetic cultures showed a stimulation of growth at all concentrations of cytikinines after 4 days (Page 245, last paragraph and Fig. 4 on page 246). R1 discusses that in the first few days, the cytokinins would stimulate growth of the organisms under study. R1 adds that the concentration of the bacterial chlorophyll and of carotenoids apparently depend on the number of cells (page 248, Discussion, first and second paragraphs).

10. Given that cytokinins stimulate growth, the activation of AMP-activated protein kinase of the microorganism or the increase in the uptake of a carbohydrate will be inherent in the stimulation process.

11. R1 discloses a fermentation in which synthetic cytokinins, kinetin and 6-benzyladenine increase the growth rate and the concentration of pigments. Given that the increase in growth rate and concentration of pigments is due to the presence of cytokinins as compared to a fermentation where cytokinins are absent, the limitation "effective to increase conversion of one or more products in the fermentation medium to a desired product as compared to conversion in a medium without the cytokinin containing preparation using otherwise identical fermentation conditions" in claims 1 and 14 is met.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 6-7, 10-13 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Romanow et al. (1969, Effect of synthetic cytokinins on growth and pigment formation by *Rhodospirllum rubrum*; hereinafter R1, Examiner's Translation) in view of Challice (1985, Purification of cytokinins on a polyvinylpyrrolidone column followed by analysis on a reversed phase C18ODS HPLC system).

14. R 1 disclosure is hereby incorporated by reference as outlined in paragraphs 6-10 above.

15. While R1 mentions that natural and synthetic cytokinins stimulate the cellular division (page 243, lines 3-4); it is silent regarding the plant source of cytokinin improving the growth and/or metabolism rate of microorganisms.

16. R2 teaches that cytokinins, as a class, can be separated from co-occurring phenolics by column chromatography using polyvinylpyrrolidone (PVP) with methanol as eluant. Subsequent fractionation of cytokinins may be achieved by HPLC. The separation system has been used to separate 2 unknown cytokinins from seedlings of *Hordeum vulgare* cv Steptoe (barley).

17. While the combined references teach the effect of cytokinins on *Rhodospirillum* for growth stimulation, it would be obvious to those skilled in the art that an organism such as *Saccharomyces* may be equally affected and as a result the processes involving Saccharomyces such as alcohol fermentation and bread dough leavening would benefit from this effect.

18. It would have been obvious to one of ordinary skill in the art, at the time the invention was made, to modify the teachings of R1 and replace the cytokinin source with barley extract containing cytokinin as taught by R2. One would do so to benefit from a plant source of cytokinin to improve the growth and/or metabolism rate of microorganisms which are important in industrial fermentations such as alcohol fermentation and bread dough leavening. Absent any evidence to contrary and based on the combined teachings of the cited references, there would be a reasonable expectation of success in using barley cytokinins to increase the growth and/or metabolism rate of microorganisms as presently claimed.

Response to Arguments

Applicants' arguments have been thoroughly reviewed. These arguments do not deem persuasive for the following reasons:

1. Regarding the rejections under 35 USC 102(b).

Applicants argue that the cited reference (R1) fails to teach each and every element of the claims.

a. Applicants are referring to the phrase "effective to increase conversion of one or more products in the fermentation medium to a desired product as compared to conversion in a medium without the cytokinin containing preparation using otherwise identical fermentation conditions" which is an amended limitation in claims 1 and 14.

R1 discloses a fermentation in which synthetic cytokinins, kinetin and 6-benzyladenine increase the growth rate and the concentration of pigments. The increase in growth rate and concentration of pigments is due to the presence of cytokinins as compared to a fermentation where cytokinins are absent. Therefore, all elements of the claims are being addressed. The Examiner is assuming that " the conversion of one or more products in the fermentation medium to a desired product" as presently claimed is meant to be the conversion of one or more substrates in the fermentation medium to a desired product.

2. Applicants argue that the alleged inherency in the rejection of claims 8-9 lacks factual support.

a. A natural phenomenon such as activation of an AMP-activated protein kinase by cytokinin is being claimed. When yeast is exposed to cytokinins, the protein kinase is activated. This is a mechanism inherent in the yeast when exposed to cytokinins. Moreover, a protein kinase, SNF1, functions as a regulator to depress many Glucose repressed genes. A gene designated WPK4 which encodes a SNF1 related protein kinase has been isolated from wheat. Cytokinins have been shown to up-regulate the accumulation of WPK4 transcripts. Therefore, the transcriptional activation of WPK4 is mediated by cytokinins. Consequently, the SNF1 related protein kinase activation is mediated by cytokinins.

Further, given that R1 discloses use of cytokinin in amount identical to that presently claimed, it is clear that the cytokinin is present in concentration effective to increase

uptake of carbohydrate or to activate an AMP -activated protein kinase of the microorganism.

3. Regarding rejections under 35 USC 103.

Applicants argue that the references fail to teach all claimed elements.

a. The disclosure by R1 has been outlined in the rejection section of the Office Action. The elements disclosed by R1 were outlined under 1a. Those elements are fermentation, product increase, cytokinins, as claimed in claims 1 and 14. R1 addresses all those elements.

4. Applicants argue that R1 teaches away from the claimed subject matter because any increase in the carotenoids is due to an increase in the cell number rather than due to an increase in fermentation.

a. Fermentation is a general term. Fermentation can encompass the production of the cell mass, a primary metabolite, a secondary metabolite or both. Therefore, increase in the number of cells as reported by R1 is an increase in fermentation. This increase in the cell mass is related to the increase in the concentration of carotenoids. It is clear that cytikinins have caused an increase in fermentation.

5. Applicants argue that Challice is entirely silent on the issue of fermentation and merely teaches the isolation of natural cytokinins.

a. Please note that while Challice (R2) does not disclose all the features of the present claimed invention, Challice is used as teaching reference, and therefore, it is not necessary for this secondary reference to contain all the features of the presently claimed invention, *In re Nievelt*, 482 F.2d 965, 179 USPQ 224, 226 (CCPA 1973), *In re*

Keller 624 F.2d 413, 208 USPQ 871, 881 (CCPA 1981). Rather this reference teaches a certain concept, and in combination with the primary reference, discloses the presently claimed invention.

6. Applicants argue that the cited references lack suggestion or motivation and that there is no motivation to produce a fermentation medium as claimed in claims 6-7.

a. The requirement for the fermentation medium which should contain a cytokinin is clearly set forth by R1 and choosing a natural cytokinin from barley can be initiated by those of skill in the art as taught by R2.

7. Applicants argue that the increase in cell growth as observed in a phototrophic prokaryotic organism can not be concluded to apply in a heterotrophic eukaryoutic organism. They also disagree with the alleged cross-kingdom effect.

a. Applicants are provided with the following references where cytokinin and kinetin have been used to increase fermentation rates.

A. US 3, 317, 404: Production of metabolic products of Gram positive bacteria by the addition of kinetin to the fermentation broth.

B. DD 148889. Protein rich yeast production by conventional fermentation in the presence of cytokinin or cytokinin-like substances especially kinetin. This document is in German. However, the English abstract is also included.

Therefore, it is clear that cytokinin has a cross-kingdom effect.

Conclusion

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to HAMID R. BADR whose telephone number is (571)270-3455. The examiner can normally be reached on M-T 5:30 to 4:30 (Friday off).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Callie Shosho can be reached on (571) 272-1123. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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